IN THE UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF TENNESSEE
NORTHEASTERN DIVISION AT COOKEVILLE

ANDREW SCOTT RODRIGUEZ,	)	
	)	
Plaintiff,	)	
	)	
v.	)	**Civil Action No. 2-08-0124**
	)	
STRYKER CORPORATION, et al.	)	

STRYKER'S MEMORANDUM IN SUPPORT OF MOTION TO EXCLUDE DR. SANDER GREENLAND UNDER FRE 702 AND *DAUBERT*

Despite already extensive expert witness disclosures, plaintiff added new expert "rebuttal" witnesses, including epidemiologist Dr. Sander Greenland. Not only is the proposed testimony improper rebuttal (*see* Mot. to Exclude Rebuttal Experts, filed concurrently with this motion), Dr. Greenland's testimony also fails to meet the standards for admissibility under Federal Rule of Evidence 702, and *Daubert v. Merrell Dow Pharm, Inc.,* 509 U.S. 579 (1993) (*Daubert I*) and its progeny.

In deposition testimony in another case, Dr. Greenland disavowed the very opinions he proposes to submit to the jury in this case. In addition, Dr. Greenland's opinions have not been subjected to peer review and, by his own admission, would not withstand peer review. Finally, Dr. Greenland generated his opinions solely for litigation, and those opinions are not generally accepted in the scientific community.

SUMMARY

Plaintiff proposes Dr. Greenland to testify regarding general causation in support of the claim that plaintiff developed chondrolysis of the shoulder after using a pain pump for administration of anesthetic into the intra-articular space of his shoulder joint. Dr. Greenland's

report attempts to mathematically analyze chondrolysis case series developed by other scientists, and he concludes that "the most likely explanation" for the associations seen "between chondrolysis and intra-articular high-flow pain-pump catheters … is that these pumps are a primary and essential contributing factor to the development of chondrolysis in the cases…." (Greenland Rebuttal Report ("Rebuttal Rpt."), October 12, 2010, pg. 40, Declaration of Robert Connolly in Support of Defendants Stryker Corporation and Stryker Sales Corporation's Motion to Exclude Dr. Sander Greenland Under Federal Rule of Evidence 702 and Daubert ("Connolly Decl."), Exh. A.) Although the Rebuttal Report is the first report from Dr. Greenland that plaintiff submitted in this case, the Rebuttal Report incorporates by reference and purports to supplement earlier August and November 2009 reports produced in other litigation. (Greenland August 2009 Report ("August 2009 Rpt."), Greenland November 2009 Report ("Nov. 2009 Rpt."), Connolly Decl., Exhs. B and C.) The newest report's conclusions vary only slightly from the previous reports.

Any effect that any of Dr. Greenland's expert reports might have otherwise had on the issue of general causation is undone by his prior testimony in a pain pump action entitled *Cox, et al. v. DJO, LLC, et al.*, in which he recanted the 2009 reports' already-limited conclusions and admitted that he cannot say whether continuous infusion had *any* role in the chondrolysis observed in the case series he examined. (Deposition Testimony of Sander Greenland, "Greenland at," September 24, 2009, *Cox, et al. v. DJO, LLC, et al.*, Case No. CV07-1310AA, District of Oregon; Connolly Decl. at Exh. D.) Just as important, Dr. Greenland admitted that whatever conclusions he could reach were applicable only to the case series he reviewed and could not be applied to the general population, let alone the plaintiff herein.

Nothing in the supplemental report alters the inconsistencies between Dr. Greenland's

Cox depositions and his expert reports. Greenland does not maintain that anything new changes his previous *Cox* deposition testimony, where he admitted that there was no direct link between chrondrolysis and continuous infusion. And he does not claim that his conclusions can be applied to the general population. For these reasons, Dr. Greenland's opinions are irrelevant to the issue of causation and to this litigation, and should be excluded on those grounds alone. Indeed, Greenland's 2009 reports have already been excluded by Chief Judge Ann Aiken in the District of Oregon following rigorous scrutiny.

But the defects in Dr. Greenland's testimony do not end there. His reports and opinions have no predicate in his pre-litigation research, but rather were generated exclusively for his proposed expert testimony. In addition, his opinions were never subjected to the scrutiny of the scientific community and, by his own admission, would not withstand peer review. Finally, Dr. Greenland's opinions are not generally accepted in the scientific community. For these reasons, his opinions, including those rebutting and criticizing defendants' expert's testimony, exhibit a glaring lack of the indicia of reliability inherent in good science and should be excluded.

ARGUMENT

I. Dr. Greenland's opinions are irrelevant because he does not conclude that continuous infusions cause chondrolysis in the general population, let alone that they caused chondrolysis in plaintiff.

Federal Rule of Evidence 702 governs the admissibility of expert testimony. It allows a qualified expert to present testimony that "will assist the trier of fact" in understanding the evidence or in determining a factual issue, provided "(1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case." Here, Dr. Greenland's opinion does not meet the fundamental requirement of "assist[ing] the trier of fact" because he does not conclude continuous infusion causes chondrolysis. *See Pride v. BIC Corp.*,

218 F.3d 566, 578 (6th Cir. 2000) (expert testimony must assist the trier of fact). More importantly, his opinion goes no farther than a causal inference between continuous infusion and chondrolysis *in the patients in the specific case studies he chose to examine*. In other words, his opinion is entirely limited to the patients in those studies and he is not extrapolating or opining on the general populations of shoulder arthroscopies or to plaintiff's specific circumstances.

In Dr. Greenland's earliest August 2009 report – produced for the first time here in October 2010 – Dr. Greenland's causation opinion was strangely circumscribed, going no further than an "inference" that continuous infusion was a "contributing factor" in chondrolysis. (August 2009 Rpt. at 1; Connolly Decl, Exh. B.) In fact, he never offered even an initial general causation opinion, specifically limiting his conclusions to "the development of chondrolysis in the cases reported by *Hansen et al. and by Dr. Matsen*." (*Id.*) Since the initial report, Greenland has only slightly modified his initial conclusions. Even now, by his own specific limitations, Dr. Greenland has not opined as to the causation of chondrolysis *in general*. (Rebuttal Rpt. at 39; Connolly Decl., Exh. A.) This hedging demonstrates a latent uncertainty that was previously brought to light at Dr. Greenland's deposition in the *Cox* case.

Under deposition questioning in the *Cox* matter, Dr. Greenland acknowledged that the Hansen study, the "key" study in the 2009 reports, contained manifold biases and confounding factors for which there were no controls. (Greenland at 166:11-168:17, Connolly Decl., Exh. D.) In his most recent supplemental report, Dr. Greenland continues to focus more on the Hansen study than any of the other cases studies. But in *Cox*, Greenland admitted that all he really knew was that the Hansen study contained a morass of potentially contributory factors, none of which he could say was causative:

> All I have is … all the details that you laid out, that that combination shows this huge association with the outcome, and that could be because

> it's one of the factors in there or some interaction of two of the factors in there, and I could not make a separate statement about any of them based on the data that I have seen.

(Greenland at 303:6-16, Connolly Decl., Exh. D.) *By the end of his deposition, he voluntarily admitted his realization that chondrolysis might well be completely unrelated to continuous infusion:*

> [I]t could be that whenever they did the pain pump … they also used a particular kind of suture … and that suture was responsible. So what I'm trying to tell you is that you've emphasized to me that without further data, there is no way to be sure that it isn't some aspect of something surrounding … what they did always when they used the pain pumps and didn't do when they didn't use those intra-articular pain pumps ….

(Greenland at 322:2-323:5, Connolly Decl., Exh. D.)

Furthermore, while basing his opinion on the Hansen study, Dr. Greenland admitted that he never analyzed the underlying data or performed independent analysis of potential biases or confounding factors. (Greenland at 128:24-129:20; 167-168; Connolly Decl., Exh. D.) To this day, Greenland has not actually analyzed the underlying data or performed independent statistical analysis of potential biases or confounding factors in *any* of the studies in his reports—he just implies that an analysis of confounding factors is not necessary. (Rebuttal Rpt. at 10; Connolly Decl., Exh. A.) As stated by the Sixth Circuit, "[b]efore any inferences are drawn about causation, the possibility of other reasons for the association must be examined, including chance, biases such as selection or informational bias, and confounding causes." *Nelson v. Tenn. Gas Pipeline Co.,* 243 F.3d 244, 253 (6th Cir. 2001) (citing Reference Manual on Scientific Evid. 333, 354 (2d ed. 2000)). Because Greenland does not statistically analyze confounding factors or the underlying data, he cannot demonstrate causation.

Moreover, Greenland acknowledges that review of the underlying data is a component of good epidemiological study. (Greenland at 174:1-9,179:11-180:10, Connolly Decl., Exh. D.)

Thus, Dr. Greenland is proffered as a general causation expert who never analyzed the data upon which his limited conclusion is based, who cannot conclude that continuous infusion is even a contributory factor in chondrolysis, and who voluntarily admits that the condition may be completely unrelated to continuous infusion.

Moreover, during his *Cox* deposition, Dr. Greenland acknowledged the epidemiological concept of "generalizability," which he defined to mean whether the results of the study of one small population are transferable to another population. (Greenland at 272:6-19, Connolly Decl., Exh. D.) He admitted that his opinion did nothing to determine whether the results of the Hansen study were generalizable to the general population. (Greenland at 272:23-273:1, Connolly Decl., Exh. D.) As a result, he agreed that he had nothing to say regarding the causation of chondrolysis amongst the general population and his conclusions were limited to the Hansen study. (Greenland at 275:11-22, Connolly Decl., Exh. D.) Likewise, his supplemental reports, including the rebuttal report produced in this case, are limited to the case series discussed in the reports. Dr. Greenland stated that he would "infer that the most likely explanation for the enormous associations seen in the literature between chondrolysis and intra-articular high-flow pain-pump catheters eluting bupivacaine with ephinephrine is that these pumps are a primary and essential contributing factor in the development of chondrolysis *in the cases seen…above*." (Rebuttal Rpt. at 40, Connolly Decl., Exh. A.) As a result, none of Dr. Greenland's reports contain conclusions having any bearing on the issue of whether continuous infusion is capable of causing chondrolysis in the general population, or in the plaintiff.

"Scientific evidence must [] meet the [Daubert] 'fit' requirement by having a valid scientific connection to the inquiry at issue in the case." *Daubert v. Merrell Dow Pharmaceuticals, Inc*., 43 F.3d 1311, 1317 (9th Cir. 1995) ("Daubert II"). A valid scientific

connection between the proffered expert testimony and the case is crucial, because "[s]cientific expert testimony introduces special dangers to the fact-finding process." *Cloud v. Pfizer Inc*., 198 F.Supp.2d 1118, 1130 (D. Ariz. 2001). "[I]t can be both powerful and quite misleading because of the difficulty in evaluating it. Therefore, federal judges must exclude proffered scientific evidence under Rule 702 unless they are convinced that it speaks clearly and directly to an issue in dispute in the case, and that it will not mislead the jury." *Id*.

Here, Dr. Greenland has glittering credentials and a C.V. that threatens to run into triple digits. Yet, as set forth above, a close reading of his expert reports and his *Cox* deposition testimony demonstrates that he cannot conclude that continuous infusion is generally capable of causing chondrolysis and, in any event, has nothing to say that is applicable to the general population or plaintiff in particular. Dr. Greenland's testimony has no valid scientific connection to causation issues in this case, but it does raise a substantial risk that the jury will believe him solely because of his qualifications.

Recognizing the limitations to Dr. Greenland's opinion, following extensive briefing and lengthy Daubert hearings, Chief Judge Aiken in the District of Oregon determined that Dr. Greenland's limited opinions should be excluded. In considering Dr. Greenland's August and November 2009 reports, Judge Aiken concluded that Dr. Greenland's causation opinion would not "aid the jury's determination of causation." *McClellan v. I-Flow Corp*., 2010 WL 1753261 at *43 (D. Or. April 29, 2010). The Court found that the testimony of Dr. Greenland (and Dr. Wells) was not "particularly helpful or relevant, given their inability to generalize the stated association beyond the patients involved in the Hansen/Beck Study" and that their testimony "would likely confuse or mislead rather than assist the jury under Fed. R. Civ. P. 403." *Id*. at *42. The same analysis applies to this case as Dr. Greenland is still unable to generalize the

stated associations beyond the patients involved in the case series he considers. As a result, this Court should exclude Dr. Greenland's opinions.

II. Dr. Greenland's opinion lack the indicia of reliability inherent in good science.

A. Dr. Greenland's opinions are litigation-driven.

Dr. Greenland conceded that he conducted the research and investigation into the causation of chondrolysis solely within the context of, and for, litigation. (Greenland at 11:2-6, Connolly Decl., Exh. D.) This is a "very significant fact" that weighs against him in the determination of whether his opinion is reliable. *Daubert II*, 43 F.3d at 1317. Indeed, the Sixth Circuit has recognized repeatedly that when expert opinions are prepared solely for purposes of litigation they should be viewed with some caution, and in such instances it is within a trial judge's discretion to apply the Daubert factors with greater rigor. *Johnson v. Manitowoc Boom Trucks,* 484 F.3d 426, 435 (6th Cir. 2007); *see also Mike's Train House, Inc. v. Lionel, L.L.C.*, 472 F.3d 398, 408 (6th Cir. 2006) ("We have been suspicious of methodologies created for the purpose of litigation."); *Rose v. Matrixx Initiatives, Inc.*, 2009 WL 902311 at *16 (W.D. Tenn., March 31, 2009) (excluding general causation opinions of an expert which were developed in the course of litigation).

In situations where expert opinions are developed solely for litigation, like those of Dr. Greenland, they are more likely to have been biased toward a particular conclusion, and are less likely to have been constructed to meet the "variety of standards" endemic to the expert's chosen scientific field. *Daubert II*, 43 F.3d at 1317. Thus, Dr. Greenland's concession in *Cox* that his opinions are litigation-driven highlights the fact that his opinions are lacking "important, objective proof that [his] research comports with the dictates of good science." *Id.*

B. Dr. Greenland's opinions have not been subjected to peer review.

Dr. Greenland admitted in his *Cox* deposition testimony that he has not submitted his

opinions for peer-review and has no intention of doing so. (Greenland at 138:17-25, Connolly Decl, Exh. D.) In fact, he candidly conceded that no peer-reviewed journal would accept them without a lot more work or a lot more caution in the conclusions. (Greenland at 296:14-297:17, Connolly Decl., Exh. D.) Peer review and publication provide "a significant indication … that [an opinion] meets at least the minimal criteria of good science." *Daubert II*, 43 F.3d at 1318. "If nothing else, [they] increase the likelihood that substantive flaws in methodology will be detected." *Id.; see also Nelson v. Tenn. Gas Pipeline Co.,* 243 F.3d 244, 251 (6th Cir. 2001) (The lack of peer review "was plainly relevant to the determination of whether Kilburn's causation theory was based upon good science."). Dr. Greenland's acknowledgment that his opinion is unfit for publication is a tacit admission that it fails to meet the standards of good science. *Id*. Dr. Greenland's opinions have not been subjected to peer review.

C. Dr. Greenland's opinions lack the intellectual rigor characteristic of his professional efforts.

As the Supreme Court stated in *Kumho*, the objective of the district court's gatekeeping responsibility under *Daubert* "is to ensure the reliability and relevancy of expert testimony. It is to make certain that an expert … employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field." *Kumho Tire Co., Ltd. v. Carmichael*, 526 U.S. 137, 152 (1999); *Best v. Lowe's Home Centers, Inc*., 563 F.3d 171, 177 (6th Cir. 2009) (same). Dr. Greenland's testimony falls below that threshold. As discussed above, Dr. Greenland provides no independent statistical analysis of the underlying data used in the case series and studies cited in his expert reports. Further, as his extensive and impressive C.V. demonstrates, he has no compunction about publishing on just about any topic within his expertise. (Rebuttal Rpt., Connolly Decl., Exh. A.) Yet he has already admitted that his earlier expert reports would not survive the peer-review process without substantially bolstering either

its science or its disclaimers. (Greenland at 296:14-297:17, Connolly Decl., Exh. D.) He thus concedes a substantial deficit between his intellectually rigorous epidemiology practice and his flaccid causation opinion as a paid expert. This gap is impermissible under *Kumho*.

D. Dr. Greenland's opinions are not generally accepted by the scientific community.

Widespread acceptance of a theory in the scientific community "can be an important factor in ruling particular evidence admissible." *Daubert I*, 509 U.S. at 594; *Nelson v. Tennessee Pipeline Co.*, 1998 WL 1297690 at *7 (W.D. Tenn. 1998). Indeed, "[m]any courts have recognized that an [expert opinion's] unexplained conflict with the generally accepted [] theories in a given scientific field can be a basis for excluding proffered expert testimony." *Hall v. Baxter Healthcare Corp*., 947 F. Supp. 1387, 1406 (D. Or. 1996). Thus, when an expert asserts a causal relationship between a product and disease, but does not explain why the relevant scientific literature contains "no studies [that] have established a causal link of any scientific significance," his testimony is unreliable and inadmissible. *Id*. at 1406-07; *see also Domingo v. T.K., M.D*., 289 F.3d 600, 606 (9th Cir. 2002) (upholding exclusion of expert's testimony in part because "there was no evidence of widespread acceptance" of the expert's theory linking the alleged cause and effect).

In his *Cox* deposition testimony, Dr. Greenland grudgingly admitted that no published article has concluded that continuous infusion causes chondrolysis; he even noted that "not even the Hansen study makes that conclusion." (Greenland at 136:9-137:18, Connolly Decl., Exh. D.) Since then, Dr. Greenland has testified in other matters regarding the studies he cites in his reports, admitting that studies such as the Rapley study (cited in the rebuttal report) did not conclude that there is a cause and effect relationship between the use of pain pumps and the development of chondrolysis. (Deposition Testimony of Sander Greenland in *Suhn, et. a. v.*

BREG, Inc., et al., Case No. 4:08-cv-04190-LLP, District of South Dakota, Feb. 24, 2010, Connolly Decl., Exh. E.) Despite the fact that Dr. Greenland concedes that the relevant scientific literature contains no studies that have established a causal link of any scientific significance between continuous infusion and chondrolysis, he makes no effort to explain the discrepancy between these studies and his general causation theories. *See Conde v. Veliscol Chem. Corp*., 804 F.Supp. 972, 1024 (S.D. Ohio 1992) (when expert expresses an opinion that is not generally accepted within the medical and scientific communities, he has an obligation to provide a reasoned explanation of why his methodology and opinions differ from those representing the collective view of the relevant medical or scientific disciplines).

Like his 2009 reports, Dr. Greenland's rebuttal report does not cite any new studies which demonstrate a statistically significant causal link between continuous infusion and chondrolysis. In both Dr. Greenland's own deposition testimony and the case series themselves, the lack of a causal tie between continuous infusion and chondrolysis is clear. (Anderson Report at 460 (stating that the authors could not establish a causal link), Connolly Decl., Exh. F.) Because Dr. Greenland does not explain the discrepancy between his causation theory and the relevant literature, his testimony should be excluded.

III. Dr. Greenland's opinions are based on unreliable data.

In addition to the numerous deficiencies in the Hansen case series, Dr. Greenland relies on multiple animal studies, case series, and case reports which fail to meet the indicia of reliability. Because Dr. Greenland's opinions are based on unreliable data, his testimony should be excluded.

A. The Matsen/Wiater study is tainted and unreliable.

Dr. Greenland's rebuttal report cites the Matsen/Wiater study[1], although the bulk of his opinion on these studies is contained in the initial 2009 reports. The Matsen/Wiater study is irreparably tainted. Dr. Greenland attempted to add the Matsen/Wiater case study as an additional basis in his November 2009 supplemental report. But, Chief Judge Aiken in Oregon held that no expert, including specifically Dr. Greenland (and Dr. Wells), would be permitted to express any opinion based on the Matsen/Wiater study. *McClellan v. I-Flow Corp*., 2010 WL 1753261 at *13, n.9, *31, n. 24. (D. Or. April 29, 2010). Judge Aiken found that the testimony of Dr. Matsen, whose opinions on chrondrolysis rested solely on his case study with Dr. Wiater, were "irreparably tainted by litigation bias and unreliable." *Id.* at *31. Judge Aiken set forth in detail the bases for the exclusion of Dr. Matsen's testimony and of the Wiater study. *Id*. at *24-*31. After assessing the impermissible litigation taint and involvement of vested interest plaintiffs' counsel in the study, the Court aptly concluded: "At best, Dr. Matsen sought 'clarification' from [plaintiff's counsel] concerning his analysis of the patient data. At worst, [plaintiff's counsel] utilized Dr. Matsen in an orchestrated attempt to design, conduct, and complete a research study for the purpose of supporting litigation in which he has a vested economic interest." *Id* at 31.

This Court should exclude Dr. Greenland's reliance on the litigation-tainted study of Wiater et al.

B. Dr. Greenland's reliance on and extrapolation from various other studies is also unreliable.

While defendants do not dispute that an expert may consider animal studies, in vitro

[1] The Matsen/Wiater study, which is referred to by Dr. Greenland in his supplemental report as the Wiater, et al. study, is also known as the "396-patient study." Its genesis and development is set forth in *McClellan v. I-Flow Corp*., 2010 WL 1753261 at *24-31.

studies, case reports, and other scientifically valid information that helps to advance the search for answers to the chondrolysis question, fatal reliability flaws arise when the analytical gap between an opinion and supporting data grows too large and the underlying data support the opinion only by the *ipse dixit* of the expert. *General Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997); *Nelson v. Tenn. Gas Pipeline Co.,* 243 F.3d 244, 253-54 (6th Cir. 2001) (too great an analytical gap existed between the data and the opinion that PCBs can cause a brain disorder). Scientific consideration becomes unjustified extrapolation when experts draw conclusions detached from the data upon which they purport to rely. *E.g.*, *Domingo v. T.K.*, 289 F.3d 600, 606-07 (9th Cir. 2002).

Dr. Greenland reaches his limited general causation opinion only through unjustified extrapolation from the available scientific studies and data, because medical science currently does not know the cause, progression, and prevention of chondrolysis and can only hypothesize about whether continuous infusion plays a role in causing the disorder. *See Rose v. Matrixx Initiatives, Inc.*, 2009 WL 902311 at *12 (W.D. Tenn., March 31, 2009) (expert's extrapolation of findings from a polio study and his application of those findings to the action was not reliable). A review of the oft cited literature illustrates that the proffered causation opinions connect to that data only by the "unadorned assertions" of the experts themselves. *Daubert II,* 43 F.3d at 1319.

1. <u>In vitro studies</u>

Dr. Greenland relies upon several in vitro studies, including studies published by Karpie et al., and Chu et al. (Rebuttal Rpt. at 22, Connolly Decl., Exh. A). Those studies support causation only if an expert improperly extrapolates from them to reach his opinion.

The Karpie article does not support causation. It discusses an in vitro study of cytotoxic

effects of lidocaine on bovine articular chondrocytes. The article recognizes the differences in toxicity between lidocaine and bupivicaine: "With a molecular weight of 234.34 g/mol, lidocaine is smaller than bupivicaine is (molecular weight, 342.9 g/mol) and may therefore have greater potential to penetrate the intact articular surface." (Connolly Decl., Exh. G at 5). The article cautions *against* extrapolating its conclusions to humans: "As this study was performed using chondrocytes obtained from healthy bovine cartilage, the results may be different with human cartilage after joint injury or in the presence of degenerative changes." (*Id*. at 6.) It advocated additional "in vivo studies designed to model each potential clinical scenario. . . ." (*Id.*)

The Chu articles state similar limitations. (Connolly Decl., Exh. H at 698 ("limitations were that this was an in vitro study that used bovine cartilage, and there was no dose-response curve"); *id*. (stating that data presented supports "need for comprehensive additional studies"); *id.,* Exh. I at 819) ("one of the limitations of our study was that human cells could not be considered to be as healthy as bovine cells"); *id*. at 819-20 ("Diseased chondrocytes could be more susceptible to the effects of cytotoxic agents."); *id.* at 820 ("It is important to note that in vitro assessments do not account for dilutional effects or in vivo reparative processes.").)

The in vitro studies cited by Greenland do not reliably support causation conclusions. *See Turpin v. Merrell Dow Pharms., Inc*., 959 F.2d 1349, 1360 (6th Cir. 1992) (excluding testimony where the record failed to make clear how animal studies were sufficient to show that Bendectin causes birth defects); *In re Bausch & Lomb, Inc. Contact Lens Solution Prod. Liab. Litig*., 2009 WL 2750462, at *12 (D.S.C. Aug. 26, 2009) (recognizing that "in-vitro tests are only the first step, and that animal studies followed by human trials are necessary to determine applicability of an hypothesis to humans" because "[i]n vitro tests generate hypotheses but lack

sufficient reliability, standing alone, to demonstrate causation in humans"); *see generally* REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 442 (Federal Judicial Center, 2d ed. 2000) (2d ed. 2000) ("REFERENCE MANUAL") ("The major barrier to use of in vitro results is the frequent inability to relate doses that cause cellular toxicity to doses that cause whole-animal toxicity.").

2. In vivo animal studies

Dr. Greenland also relies on in vivo animals studies conducted by Gomoll, et al. (August 2009 Rpt. at 12, Connolly Decl., Exh. B) Those studies likewise provide support for causation conclusions only through unjustifiable extrapolation. The first Gomoll article does not support causation conclusions. (Connolly Decl., Exh. J.) It discusses a study investigating chondrotoxicity of bupivicaine in the rabbit shoulder. The article cautions against extrapolation to humans: "One limitation of our study, which it shares with most animal models, should be considered; although we were able to show the detrimental effects of bupivicaine on the cellular and tissue level in a rabbit model, it remains to be determined whether human cartilage is equally susceptible and whether these histopathologic and functional changes result in subsequent development of rapidly progressive osteoarthritis." (Connolly Decl., Exh. J, at 817.) "Because epidemiologic study of chondrolysis in humans will require an extremely large sample size because of the low incidence and prevalence of this condition, additional studies in a larger animal model with longer-term follow-up, as well as in vitro studies with continuous exposure of human cartilage to bupivicaine, are necessary to provide further understanding." (*Id*. at 818); *see also Kilpatrick*, 2009 WL 2058384, at *6 (holding that Gomoll article does not support chondrolysis causation conclusion but instead undercuts it).

The second Gomoll article, rather than supporting causation, tends to disprove it.

(Connolly Decl., Exh. K ("Gomoll 2").) The study underlying the article continued the work reported in Gomoll's first article. (*Id*. at 72-73.) The article reported no demonstrable impairment of cartilage following infusion of local anesthetic:

> Our current study did not demonstrate any permanent impairment of cartilage function at 3 months in a rabbit shoulder model. Conversely, we found an increase in chondrocyte anabolic activity, as evidenced by an elevated sulfate uptake and higher PG content in cartilage exposed to bupivicaine when compared with contralateral controls, or with shoulders treated with saline solution. These apparently conflicting results suggest that for the experimental model used, cartilage function was only transiently impaired by exposure to bupivicaine.

(*Id*. at 75-76.) As with other scientific articles on this subject, the Gomoll 2 article recognizes that "[a]dditional experiments will be necessary before the phenomenon of bupivicaine toxicity is fully understood." (Id. at 77.) While Dr. Greenland cites the Gomoll article, the contrary results are not addressed. An expert betrays advocacy by failing to report the full scope of the relevant scientific literature, or reporting contrary literature without explaining why it does not refute his conclusions. "[I]f the relevant scientific literature contains evidence tending to refute the expert's theory and the expert does not acknowledge or account for that evidence, the expert's opinion is unreliable." *In Re Rezulin Products Liability Litig*., 369 F.Supp.2d 398, 425 (S.D.N.Y. 2005) ("*In Re Rezulin*").

The Gomoll articles do not reliably support causation opinion. *See Daubert II*, 43 F.3d at 1319 ("While these materials indicate that Plaintiff's experts have relied upon animal studies, chemical structure analyses and epidemiological data, they neither explain the methodology the experts followed to reach their conclusions nor point to any external source to validate that methodology."); *Rose v. Matrixx Initiatives, Inc*., 2009 WL 902311 at *14 (W.D. Tenn., March 31, 2009) (animal studies did not provide reliable support for expert's opinion).

3. Case reports/Case series

Dr. Greenland also relies on case reports and case series, including the Hansen study (Tab No. 26) to support his opinions. Neither the case reports or case series, however, can reliably support causation conclusions legally or substantively. Further, Dr. Greenland failed to consider case reports demonstrating other potential causes, including cases of chondrolysis where no potential cause was ascertained. Dr. Greenland's selective reliance on a few cherry-picked reports and failure to consider contrary evidence make his opinion unreliable.

As an initial matter, case reports do not support causation opinions. *Rose v. Matrixx Initiatives, Inc.,* 2009 WL 902311 at *15 (W.D. Tenn., March 31, 2009) (a case study does not prove causation and standing alone, is insufficient to establish general causation); *Cloud v. Pfizer, Inc*., 198 F. Supp. 2d 1118, 1133 (D. Ariz. 2001) ("[Case reports] are merely compilations of occurrences, and have been rejected as reliable scientific evidence supporting an expert opinion that Daubert requires"); *Brumbaugh v. Sandoz Pharm. Corp*., 77 F.Supp.2d 1153, 1156 (D. Mont. 1999) (same); *Kilpatrick*, 2009 WL 2058384, at *7 ("case reports are way down at the very bottom as far as medical strength of an article and cannot establish medical causation") (quotations omitted).

Dr. Greenland's 48-page rebuttal report is replete with references to case studies and case reports which reportedly provide support for plaintiff's causation theories—despite the fact that the studies do not demonstrate a causal link between the intra-articular pumps and chondrolysis. Given Dr. Greenland's sprawling testimony and cursory citations to the cases reports and case series, it is impossible to individually address all of the flaws in his report within a *Daubert* motion limited to 25 pages. Perhaps the most critical flaw in Dr. Greenland's report—aside from his failure to actually conclude that intra-articular pumps cause chondrolysis in the general

population or in plaintiff—is that the support for his opinions consists of case reports and case studies which do not—and cannot—establish causation. None of his case studies or case series establish the critical causal link necessary to prove plaintiff's claims. (*See* Anderson Rpt., Connolly Decl. at Exh. F.)

For example, the Hansen article does not support causation conclusions because it acknowledges that "[t]he cause of this process is unknown" and that "[p]ostarthroscopic glenohumeral chondrolysis is a devastating complication that has yet to be etiologically defined." (Connolly Decl., Exh. L at 1628, 1632.) "[F]urther investigation of the possible association of pain pump use with chondrolysis is warranted." (*Id*. at 1633.) As the court in *Kilpatrick v. Breg, Inc*., 2009 WL 2058384, (S.D. Fla. June 25, 2009) explained, in finding that the Hansen article does not reliably support a causation opinion:

> Kilpatrick, and [Plaintiff's expert] Poehling, claim that this 63% injury rate (i.e. twelve chondrolytic shoulders out of nineteen treated with pain pumps) is powerful evidence of general causation. However, the Hansen study includes no statistical analysis, and therefore no means of determining whether the findings are statistically significant, or whether it is statistically meaningful to extrapolate from the relatively small sample size. Further, the study noted that thermal energy, another suspected cause of chondrolysis, was used in four cases, but did not explain whether thermal energy contributed to or wholly accounted for the chondrolysis in those cases, beyond a vague statement that 'it [thermal energy] does not appear to be clearly proven to be the only factor in these cases.' See Hansen study (dkt # 72-3, at 14). *The study purported to identify a 'strong association' between chondrolysis and intra-articular pain pumps, but also acknowledged that '[t]hermal and/or radiofrequency, suture material, and reabsorbable suture anchors may have played a role not yet completely understood at this time*.' Id. at 15. Unlike Poehling, the Hansen study declined to reach a conclusion as to the general causation of chondrolysis. . . . *Extrapolating from the Hansen study that intra-articular pain pumps cause chondrolysis, then, effectively leaves an unexplained 40% error rate in Poehling's hypothesis. This is not the 'good science' that Daubert and Rule 702 demand*. Id. at *5-6 (emphasis added).

In addition, Dr. Greenland's selective reliance on purportedly supportive literature while

ignoring published works with contrary data and conclusions exhibits a "disregard and lack of explanation for contrary findings" that renders his opinion excludable. *Carnegie Mellon Univ. v. Hoffman LaRoche, Inc.*, 55 F.Supp.2d 1024, 1039 (N.D. Cal. 1999). In *Nelson v. Tenn. Gas Pipeline Co.,* 243 F.3d 244, 253 (6th Cir. 2001), the Court affirmed the exclusion of an expert's opinions, in part, because "the record was 'replete' with evidence of other factors or agents which may have been responsible for the symptoms suffered by the flagship plaintiffs - evidence which, it appears, [the expert] utterly ignored." Statistical analysis of case reports "conceals too much to speak directly to the issue of causation." *In re Meridia Products Liab. Litig.*, 328 F.Supp.2d 791, 807-08 (N.D. Ohio 2004).

CONCLUSION

Dr. Greenland's litigation-driven opinion is too circumscribed to be of any assistance to the trier of fact under Federal Rule of Evidence 702, and hence should be excluded entirely on that basis. In addition, Dr. Greenland's opinion is properly excluded as it is based on unreliable data, the product of unjustified extrapolation, and not generally accepted in the scientific community.

Respectfully submitted,

/s/Robert M. Connolly

Robert M. Connolly
STITES & HARBISON, PLLC
400 W. Market Street
Suite 1800
Louisville, KY 40202
Telephone: (502) 587-3400

Wendy A. Tucker
Christopher P. Norton
SEDGWICK, DETERT, MORAN & ARNOLD
801 South Figueroa Street
20th Floor
Los Angeles, CA 90017
Telephone: (213) 426-6900

Counsel for Defendants, STRYKER CORPORATION AND STRYKER SALES CORP.

807653:1:LOUISVILLE